Neovascular glaucoma in a child: an unusual presentation of medulloepithelioma

Abstract

A healthy 12 month old infant without significant medical history presented with left eye redness for one week. Ophthalmic examination showed elevated intraocular pressure with iris neovascularization in the affected eye with increased optic nerve cupping. Scleral depression revealed a ciliary body mass in the supratemporal quadrant. A large, non-pigmented, vascular mass was noted; biopsy results showed multilayered cords, tubules, and sheets resembling primitive medullary epithelium arising from the ciliary body. The patient was diagnosed with medulloepithelioma. The patient underwent enucleation of the affected eye. Medulloepithelioma is a rare but important cause of neovascular glaucoma in the pediatric population. This case will focus on the characteristics of medulloepthelioma and the differential diagnosis for a non-pigmented ciliary body mass in a child.

Keywords: ciliary body, medulloepithelioma, neovascular glaucoma

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Case

A previously healthy 12 month old infant without a significant past medical history presented with left eye redness for one week. The mother denied recent trauma, sick contact, or fever. Review of systems was negative. No past medical history and surgical history were reported. The patient did not take any medications.

On physical examination, the patient was a well appearing child. She fixed and followed, was orthophoric in primary gaze. Intraocular pressures were 12 and 36 in the right and left eye, respectively. Gross examination of the left eye was positive for conjunctival injection and poorly reactive pupil. Examination under anesthesia showed left eye with mild corneal edema and shallow anterior chamber (Figure 1). Iris neovascularization was observed, along with a ciliary body mass in the supratemporal quadrant on scleral depression. Gonioscopy showed angle neovascularization and diffuse PAS. The right eye was unremarkable.

The patient underwent MRI to examine the extent of the lesion, which showed a gadolinium enhancing lesion that corresponded to the ciliary body mass. No extraocular or intracranial lesions were noted. Systemic blood tests were performed to rule out inflammatory or infectious causes of ciliary body mass; Lyme, treponemal Ab, RPR, toxoplasmosmosis antibody, toxocara antibody were all negative. CBC showed mild microcytic anemia without eosinophilia. The patient underwent a biopsy of the lesion. The pathology reported neuroepithelial lesion with cords, tubules, and sheets arising from the medullary epithelium with mitotic activity most consistent with malignant medulloepithelioma (Figure 2). Due to the large size and vascularity of the lesion, an enucleation was performed.

Questions

- What is medulloepithelioma?
- What is the differential diagnosis for a non-pigmented ciliary body mass in a child?
- What is the management for medulloepithelioma?

What is medulloepithelioma?

Ciliary body medulloepithelioma is an intraocular neoplasm derived from the primitive ciliary body medullary epithelium, which forms the non-pigmented ciliary body epithelium. First described in histologic detail by Verhoeff in 1904, this unusual lesion was named “teratoneuroma” [1]. Fuchs in 1908 coined the term of “diktyoma” [1]. However, Grinker later on identified the cellular origin of the tumor by naming it “medullopithelioma” in 1931 [2]. Without any hereditary or racial predisposition, this childhood tumor is the second most common intraocular primary malignancy, following primary intraocular retinoblastoma [3]. Its exact population based incidence is undetermined because it is a very rare neoplasm [4]. Based on the incidence of retinoblastoma, which has been reported to be around 4.1 per million in the United States, we can infer that the incidence of medulloepithelioma is significantly lower [5]. The average onset of this disease is 4 years of age, with diagnosis typically in the first decade of life. In adults, ciliary body medulloepithelioma has only been reported in 12 cases [6]. The tumor often presents as a solitary nonpigmented lesion that occurs most commonly in the ciliary body, but can also rarely involve the iris, retina, or optic nerve. It also tends

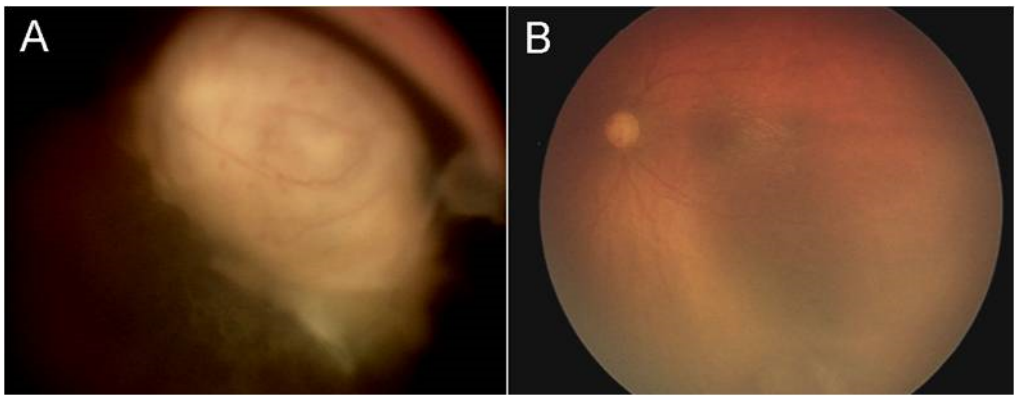

Figure 1: (A) A large vascular non-pigmented mass of the ciliary body, (B) optic nerve cupping and vascular attenuation are noted.

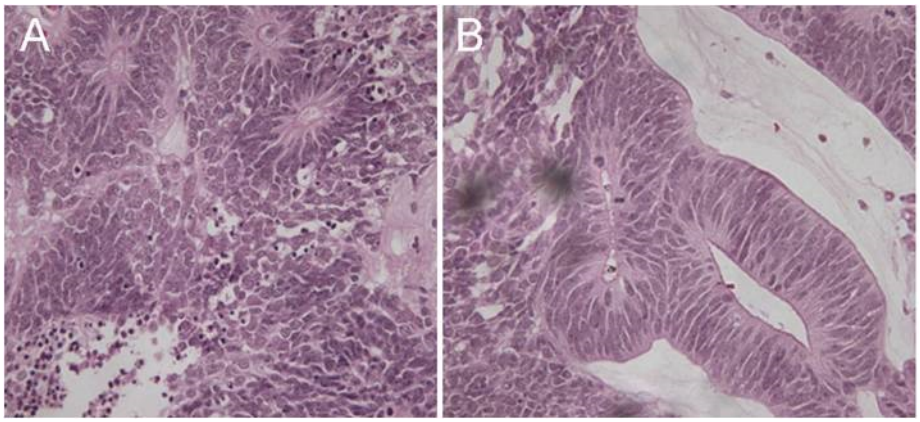

Figure 2: (A) H&E staining of tumor showing Flexner-Wintersteiner rosettes; many mitotic figures can be seen. (B) Cellular mass extends from ciliary epithelium with multilayered cords, tubules, and sheets resembling primitive medullary epithelium.

to be locally aggressive toward neighboring intraocular structures, but it rarely metastasizes [7].

Most cases of medulloepithelioma are diagnosed after the lesion has enlarged to cause anatomic displacement on neighboring structures. As in this patient, unilateral neovascular glaucoma secondary to neoplasmic proliferation is a common feature. Other presentations include lens subluxation, eye pain, conjunctival injection, ectopia lentic, secondary angle closure, uveitis, ectropion uvea, vision loss or vitreous hemorrhage [2].

Gross examinations often reveal a grey flesh colored, vascular, amelanotic lesion. Cysts can be seen on ultrasound, which are most suggestive of medulloepithelioma but biopsy is required for diagnosis [8]. Pathologic features of medulloepithelioma can be generally divided into teratoma and non-teratoma and can be further distinguished as either benign or malignant [6]. Teratoid medulloepithelioma contains heteroplastic elements such as hyaline cartilage, skeletal muscle or neuroglial tissue. On the other hand, non-teratoid medulloepithelioma is a pure proliferation of the medullary epithelium [8].

What is the differential diagnosis for ciliary body mass in a child?

A ciliary body mass in a child can include various neoplastic, infectious, or inflammatory processes. The lesion identified in this patient, which is associated with neovascularization of iris, suggests neoplastic cause. However, non-neoplasmic etiologies must be ruled out.

The presence of the ciliary mass may be secondary to chronic inflammatory lesion. Granuloma forming infection like ocular toxocariasis must be considered. Ocular toxocariasis, estimated to cause about 1 to 2% of uveitis in children, resembles retinoblastoma, coats' disease, toxoplasmic retinochoroiditis and other intraocular abnormalities [9]. Other less likely infections in this case include syphilis. Several case reports have identified masquerades of medulloepithelioma including trauma and staphyloma [10], [11], [12], [13]. Therefore, neoplastic growth must be considered high in the differential especially if symptoms do not resolve after institution of treatment.

Neoplastic lesions include retinoblastoma, medulloepithelioma, as well as Fuch's adenoma [4]. Other possibilities are more aggressive tumors like adenocarcinoma, metastatic carcinoma and amelanotic melanoma [4]. Histologic differentiation between retinoblastoma and medulloepithelioma is the presence of calcifications. Clinical and pathologic features that suggest retinoblastoma are bilaterallity (70%), calcification on pathology, genetics (40%). Medulloepithelioma is almost exclusively unilateral and generally not genetically inherited [6]. Fuchs adenoma is a reactive proliferation of the nonpigmented ciliary epithelium (NPCE) that is associated with

aging and is found in the pars placate of the ciliary body [14]. It does not present in the pediatric population.

What is the treatment?

Medulloepithelioma can be treated with local excision, enucleation, and/or radiation depending on the size of the tumor [12], [15], [16]. Attempts to treat locally have been complicated by a high rate of recurrences. Previous studies have published up to 83% recurrence in eyes with local conservative management [16]. Case studies have also reported no recurrence for 7 years and counting after local resection followed by iodine 125 brachytherapy [16]. In general, if neovascular glaucoma is noted with medulloepithelioma, then localized iridocyclectomy may not be sufficient.

Discussion

Early diagnosis of medulloepithelioma is challenging because of the difficulty of direct visualization, the rarity of the neoplasm and early age of presentation. As a result, high proportions of cases are misdiagnosed and management is delayed. Kaliki et al report that 88% of cases were initially misdiagnosed and 39 % had an additional history of treatment for erroneous diagnosis. Ultrasonographic biomicroscopy can be useful for diagnosis; the heterogenic consistency of medulloepithelioma can be detected by UBM and be used to correctly differentiate it from other solid tumors [3], [8]. Furthermore, UBM can adequately demarcate the borders of the neoplasm to aid in resection during iridocyclectomy. Biopsy and histologic studies are critical to proper diagnosis and management.

After the diagnosis of medulloepithelioma, vision sparing management is possible but requires close follow up. Recurrence of lesion may be secondary to incomplete excision. While small tumors can be locally excised and/or radiated, enucleation maybe required for large tumors and recurrent lesions.

In conclusion, medulloepithelioma is the second most common intra-ocular tumor in pediatric patients and a common presentation for neovascular glaucoma and requires a high index of suspicion to reduce the delay in diagnosis.

Final diagnosis: Ciliary body medulloepithelioma

Notes

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Competing interests

The authors declare that they have no competing interests.

Contributorship statement

All 3 authors were involved in preparing the manuscript.

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